

IN THE CLAIMS

This is a complete and current listing of the claims, marked with status identifiers in parentheses. The following listing of claims will replace all prior versions and listings of claims in the application.

1. (Currently Amended) Use of at least one of tetrahydrofolate, methylene-tetrahydrofolate and/or methyl-tetrahydrofolate, and at least one multi-targeting antifolate, for the manufacture of a pharmaceutical composition for the treatment of cancer.

2. (Currently Amended) Use according to claim 1, wherein at least 60% by weight of said THF, methyl-THF and/or methylene-THF is in the form of a biologically active isomer.

3. (Currently Amended) Use according to claim 1—or 2, wherein said multi-targeting antifolate is selected from the group consisting of premetrexed, raltitrexed, and lometrexol.

4. (Currently Amended) Use according to any one of the preceding claims claim 1, wherein said pharmaceutical composition further comprises at least one chemotherapeutic agent selected from the group consisting of anthracyclines,

New PCT National Phase Application
Docket No. 10400-000243/US
platinum derivatives, topoisomerase inhibitors, and
antimetabolites.

5. (Currently Amended) Use according to claim 1~~any one of the preceding claims~~, wherein said tetrahydrofolate, methylene-tetrahydrofolate and/or methyl-tetrahydrofolate, and said at least one multi-targeting antifolate, are formulated in different pharmaceutical compositions.

6. (Currently Amended) Use according to claim 1~~any one of the claims 1-4~~, wherein said at least one of tetrahydrofolate, methylene-tetrahydrofolate and/or methyl-tetrahydrofolate, and said at least one multi-targeting antifolate, are formulated in a common pharmaceutical composition.

7. (Currently Amended) Use according to claim 1~~any one of the preceding claims~~ wherein said cancer is selected from the group consisting of breast cancer, gastric cancer, gall bladder cancer, bile duct cancer, colon cancer, rectal cancer, liver cancer, pancreatic cancer, head and neck cancer, and mesothelioma cancer.

8. (Currently Amended) A pharmaceutical composition comprising at least one of tetrahydrofolate,

New PCT National Phase Application
Docket No. 10400-000243/US
methylene-tetrahydrofolate and/or methyl-tetrahydrofolate, and
at least one multi-targeting antifolate.

9. (Currently Amended) A pharmaceutical composition according to claim 8, wherein at least 60% by weight of said at least one of THF, methyl-THF and/or methylene-THF is in the form of a biologically active isomer.

10. (Currently Amended) A pharmaceutical composition according to claim 8-~~or~~-9, wherein said multi-targeting antifolate is selected from the group consisting of premetrexed, raltitrexed, and lometrexol.

11. (Currently Amended) A pharmaceutical composition according to any one of the claims 8 to 10claim 8, further comprising at least one chemotherapeutic agent selected from the group consisting of anthracyclines, platinum derivatives, topoisomerase inhibitors, and antimetabolites.

12. (Currently Amended) A pharmaceutical composition according to claim 8any one of the claims 8 to 11, wherein said at least one of tetrahydrofolate, said methylene-tetrahydrofolate and/or said methyl-tetrahydrofolate, and said at least one multi-targeting antifolate, are formulated in different pharmaceutical compositions.

13. (Currently Amended) A pharmaceutical composition according to ~~claim 8~~^{any one of} the claims 8 to 11, wherein said at least one of tetrahydrofolate, said methylene-tetrahydrofolate and/or said methyl-tetrahydrofolate, and said at least one multi-targeting antifolate, are formulated in a common pharmaceutical composition.

14. (Currently Amended) A kit comprising a pharmaceutical composition comprising at least one of tetrahydrofolate, methylene-tetrahydrofolate and/or methyl-tetrahydrofolate, and a pharmaceutical composition comprising at least one multi-targeting antifolate.

15. (Currently Amended) A kit according to claim 14, wherein at least 60% by weight of said at least one of tetrahydrofolate, methylene-tetrahydrofolate and/or methyl-tetrahydrofolate is in the form of a biologically active isomer.

16. (Currently Amended) A kit according to claim 14 ~~or 15~~, further comprising a pharmaceutical composition comprising at least one chemotherapeutic agent selected from the group consisting of anthracyclines, platinum derivatives, topoisomerase inhibitors, and antimetabolites.

17. (Currently Amended) A method for the treatment of cancer comprising administering to a patient a pharmaceutically active amount of at least one of tetrahydrofolate, methylene-tetrahydrofolate and/or methyl-tetrahydrofolate, and a pharmaceutically active amount of at least one multi-targeting antifolate.

18. (Currently Amended) A method according to claim 17, wherein at least 60% by weight of said at least one of tetrahydrofolate, methylene-tetrahydrofolate and/or methyl-tetrahydrofolate is in the form of a biologically active isomer.

19. (Currently Amended) A method according to claim 17-~~or~~ 18, wherein said multi-targeting antifolate is selected from the group consisting of premetrexed, raltitrexed, and lometrexol.

20. (Currently Amended) A method according to any ~~one of the claims 17 to 19~~ claim 17, further comprising administering a pharmaceutically active amount of a chemotherapeutic agent selected from the group consisting of anthracyclines, platinum derivatives, topoisomerase inhibitors, and antimetabolites.

21. (Currently Amended) A method according to any
~~one of the claims 17 to 20~~claim 17, wherein said at least one of
tetrahydrofolate, said methylene-tetrahydrofolate and/or said
methyl-tetrahydrofolate, and said at least one multi-targeting
antifolate, are administered consecutively.

22. (Currently Amended) A method according to any
~~one of the claims 17 to 20~~claim 17, wherein said at least one of
tetrahydrofolate, said methylene-tetrahydrofolate and/or
said methyl-tetrahydrofolate, and said at least one multi-
targeting antifolate, are administered simultaneously.

23. (Currently Amended) A method according to any
~~one of the claims 17 to 22~~claim 17, wherein said cancer is
selected from the group consisting of breast cancer, gastric
cancer, gall bladder cancer, bile duct cancer, colon cancer,
rectal cancer, liver cancer, pancreatic cancer, head and neck
cancer, and mesothelioma cancer.